

# **Lessons learned from COVID-19 vaccine trials**

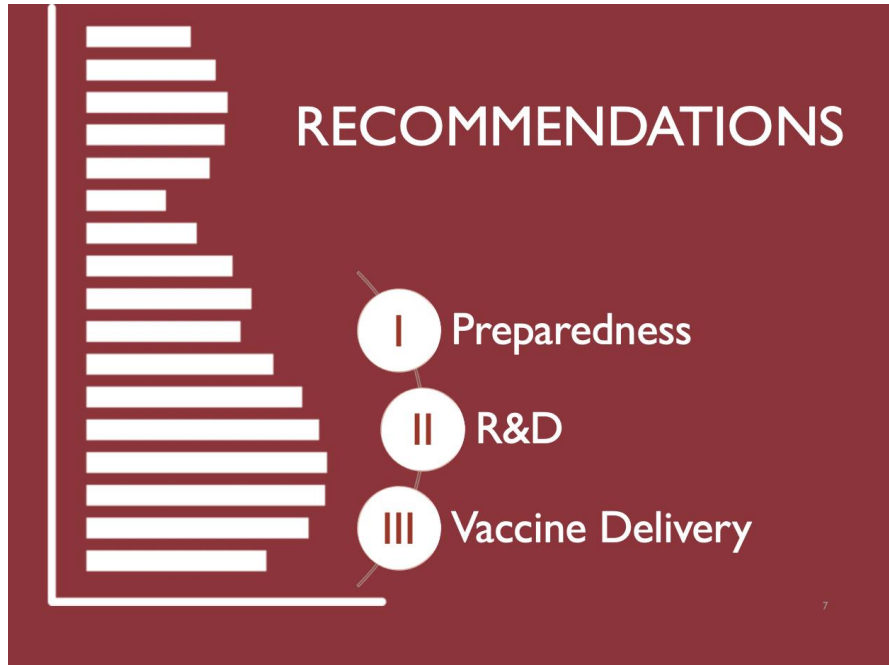
Ruth Karron  
June 17, 2022

# At the beginning of the pandemic (March 2020)

- PRGLAC recommendations had been developed and disseminated
- Value of maternal immunization well-recognized; obstacles addressed
  - Experience during the H1N1 2009 pandemic spotlighted pregnancy as a high-risk condition and the consequent value of maternal influenza immunization
  - Companies embarking on phase 3 trials of vaccines specifically developed for maternal immunization against respiratory syncytial virus (RSV)
- PREVENT (**P**regnancy **R**esearch **E**thics for **V**accines, **E**pidemics, and **N**ew **T**echnologies) guidance had been developed and disseminated

# PREVENT Guidance

- **22 Recommendations** across 3 domains to equitably and responsibly include the interests of pregnant people and their offspring in the development and delivery of epidemic vaccines



## Review

### Pregnant women & vaccines against emerging epidemic threats: Ethics guidance for preparedness, research, and response

Carleigh B. Krubiner<sup>a,1,\*</sup>, Ruth R. Faden<sup>a,b</sup>, Ruth A. Karron<sup>b</sup>, Margaret O. Little<sup>c</sup>, Anne D. Lysterly<sup>d</sup>, Jon S. Abramson<sup>e</sup>, Richard H. Beigi<sup>f</sup>, Alejandro R. Cravioto<sup>g</sup>, Anna P. Durbin<sup>b</sup>, Bruce G. Gellin<sup>h</sup>, Swati B. Gupta<sup>i</sup>, David C. Kaslow<sup>j</sup>, Sonali Kochhar<sup>k</sup>, Florencia Luna<sup>l</sup>, Carla Saenz<sup>m</sup>, Jeanne S. Sheffield<sup>n</sup>, Paulina O. Tindana<sup>o,2</sup>, The PREVENT Working Group

<https://doi.org/10.1016/j.vaccine.2019.01.011>

# PREVENT Guidance in the context of the COVID-19 pandemic

- **Recommendation #7:** Pregnant women should not be left behind as new technologies are developed
- **Recommendation #9:** Non-clinical studies required prior to clinical evaluation during pregnancy ( DART studies) should be conducted early in clinical development, as promising and appropriate candidates move to phase 2
- **Recommendation #11:** Pregnant women should have the opportunity to enroll in studies conducted during outbreaks when prospect of benefit >risk for pregnant women, their offspring, or both
- **Recommendation #17:** Pregnant women should be offered vaccines as part of an outbreak or epidemic response.

# April 2020 and beyond: early and sustained calls for inclusion of pregnant people in clinical trials for COVID-19 vaccines and therapeutics

What Pregnant Women Should Know About Coronavirus

*Mandavilli, NYT, 4/4/20*

**Consider pregnancy in COVID-19 therapeutic drug and vaccine trials**

*\*Clare L Whitehead, Susan P Walker  
The Lancet, Vol 395 May 23, 2020*

FIRST OPINION

**Pregnant and lactating women should not be excluded from Covid-19 drug, vaccine trials**

By Laura E. Riley and Brenna L. Hughes Sept. 28, 2020

*Stat*

Commentary

The need for inclusion of pregnant women in COVID-19 vaccine trials

Richard H. Beigi <sup>a</sup>  , Carleigh Krubiner <sup>b, c</sup>, Denise J. Jamieson <sup>d</sup>, Anne D. Lyerly <sup>e</sup>, Brenna Hughes <sup>f</sup>, Laura Riley <sup>g</sup>, Ruth Faden <sup>c</sup>, Ruth Karron <sup>h</sup> <https://doi.org/10.1016/j.vaccine.2020.12.074>

# Data on **risks** of COVID-19 infection and **benefits** of vaccination to both mother and infant continue to accrue

## Risk for Stillbirth Among Women With and Without COVID-19 at Delivery Hospitalization — United States, March 2020–September 2021

Weekly / November 26, 2021 / 70(47);1640–1645

On November 19, 2021, this report was posted online as an MMWR Early Release.

Carla L. DeSisto, PhD<sup>1</sup>; Bailey Wallace, MPH<sup>1</sup>; Regina M. Simeone, PhD<sup>1</sup>; Kara Polen, MPH<sup>1</sup>; Jean Y. Ko, PhD<sup>1</sup>; Dana Meaney-Delman, MD<sup>1</sup>; Sascha R. Ellington, PhD<sup>1</sup> ([View author affiliations](#))


**JAMA | Original Investigation**

## Association of SARS-CoV-2 Infection With Serious Maternal Morbidity and Mortality From Obstetric Complications

Torri D. Metz, MD, MS; Rebecca G. Clifton, PhD; Brenna L. Hughes, MD, MS; Grecio J. Sandoval, PhD; William A. Grobman, MD, MBA;

FEBRUARY 10 2022

## Placental Tissue Destruction and Insufficiency From COVID-19 Causes Stillbirth and Neonatal Death From Hypoxic-Ischemic Injury: A Study of 68 Cases With SARS-CoV-2 Placentitis From 12 Countries




David A. Schwartz, MD, MS Hyg ; Elyzabeth Avvad-Portari, MD, PhD; Pavel Babál, MD, PhD; Marcella Baldewijns, MD, PhD;

**Original Investigation | Pediatrics**

## Neurodevelopmental Outcomes at 1 Year in Infants of Mothers Who Tested Positive for SARS-CoV-2 During Pregnancy

Andrea G. Edlow, MD, MSc; Victor M. Castro, MS; Lydia L. Shook, MD; Anjali J. Kaimal, MD, MAS; Roy H. Perlis, MD, MSc

## Systematic review and meta-analysis of the effectiveness and perinatal outcomes of COVID-19 vaccination in pregnancy

Smriti Prasad<sup>1,15</sup>, Erkan Kalafat<sup>2,3,15</sup>, Helena Blakeway <sup>1</sup>, Rosemary Townsend<sup>4,5</sup>, Pat O'Brien<sup>6,7</sup>, Edward Morris<sup>6,8</sup>, Tim Draycott<sup>6,9</sup>, Shakila Thangaratinam<sup>10</sup>, Kirsty Le Doare<sup>11</sup>, Shamez Ladhani<sup>12,13</sup>, Peter von Dadelszen<sup>14</sup>, Laura A. Magee<sup>14</sup>, Paul Heath<sup>11</sup> & Asma Khalil <sup>1,5</sup> 

## Effectiveness of Maternal Vaccination with mRNA COVID-19 Vaccine During Pregnancy Against COVID-19–Associated Hospitalization in Infants Aged <6 Months — 17 States, July 2021–January 2022

Weekly / February 18, 2022 / 71(7);264–270

On February 15, 2022, this report was posted online as an MMWR Early Release.

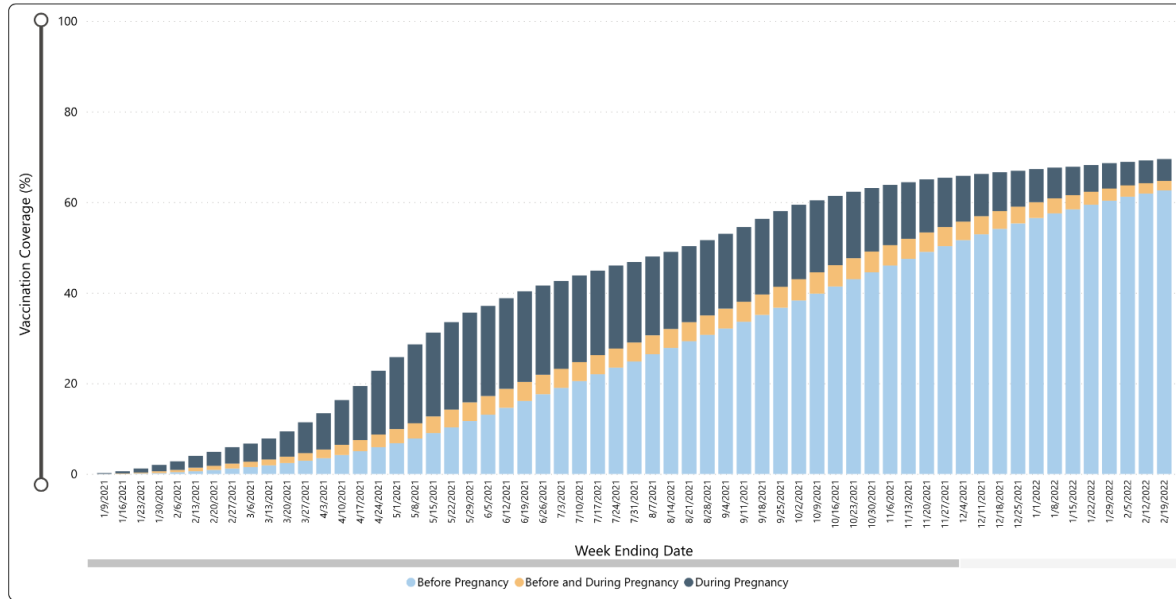
Natasha B. Halasa, MD<sup>1,\*</sup>; Samantha M. Olson, MPH<sup>2,\*</sup>; Mary A. Staat, MD<sup>3</sup>; Margaret M. Newhams, MPH<sup>4</sup>; Ashley M. Price, MPH<sup>2</sup>; Julie A. Boom, MD<sup>5</sup>; Leila C.

# PREVENT Guidance in the context of the COVID-19 pandemic

- **Recommendation #7:** Pregnant women should not be left behind as new technologies are developed **X**
- **Recommendation #9:** Non-clinical studies required prior to clinical evaluation during pregnancy ( DART studies) should be conducted early in clinical development, as promising and appropriate candidates move to phase 2 **X**
- **Recommendation #11:** Pregnant women should have the opportunity to enroll in studies conducted during outbreaks when prospect of benefit >risk for pregnant women, their offspring, or both **X**
- **Recommendation #17:** Pregnant women should be offered vaccines as part of an outbreak or epidemic response. ✓ (delayed)

# Delays in acceptance of COVID-19 vaccination during pregnancy

% of U.S. Pregnant People Fully Vaccinated with COVID-19 vaccine as of 14 June 2022



*'Excluding pregnant women from the Covid vaccine trials has resulted in pregnant women dying needlessly.'*

Professor Peter Brocklehurst, University of Birmingham, on behalf of the Commission

Healthy Mum, Healthy Baby, Healthy Future: The Case for UK Leadership in the Development of Safe, Effective and Accessible Medicines for Use in Pregnancy

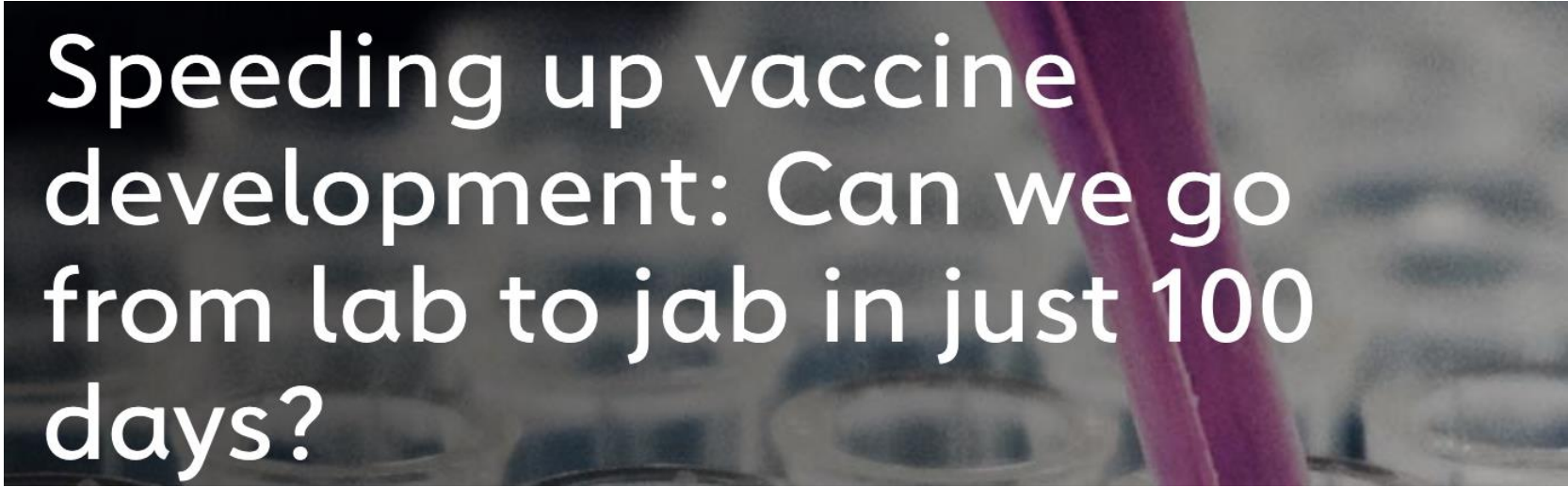
<https://covid.cdc.gov/covid-data-tracker/#vaccinations-pregnant-women>



# Toward fair inclusion: some lessons for the future

1. **Pregnant people are not at **lower** risk from infectious disease threats; they are either at **equal** or **higher** risk than their non-pregnant peers**
  - at minimum, they deserve fair access to clinical trials when benefits > risks
  - consider double benefit (pregnant person and infant)
2. **Pregnant people ≠ lactating people ≠ children**
  - “Special Population” designation may not serve the interests of any
3. **An environment favorable to maternal immunization and with sufficient financial resources was insufficient to foster timely inclusion of pregnant people in COVID-19 vaccine trials during a PHE, even as historic efforts were made to enhance diversity and inclusion of other populations.**
4. **Based upon this experience, legislative remedies should be considered to ensure fair inclusion of pregnant and lactating people in clinical trials.**

# ***Future epidemics/pandemics may increase the risk of inequity for pregnant persons***



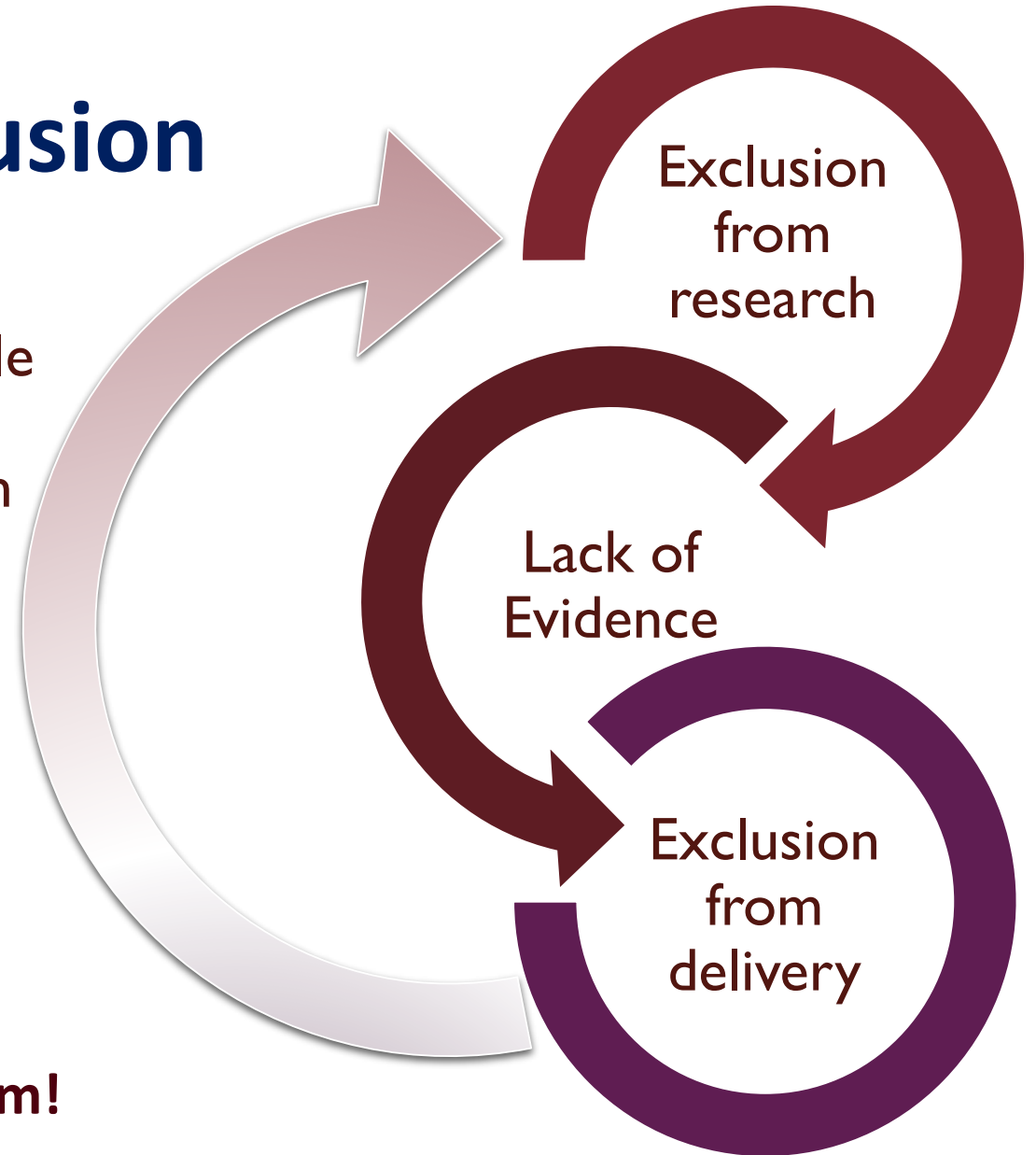
Speeding up vaccine development: Can we go from lab to jab in just 100 days?

[www.gavi.org](http://www.gavi.org)

**Extra slides**

# The Presumption of Exclusion

perpetuated cycle  
of exclusion and  
evidence gaps on  
products and  
platforms



**Morally unacceptable... need a new paradigm!**

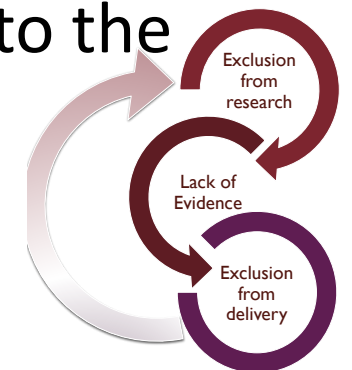
# The Presumption of Inclusion: a virtuous cycle



## ***What have we learned about data-driven policy decisions?***

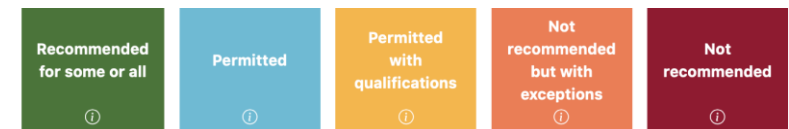
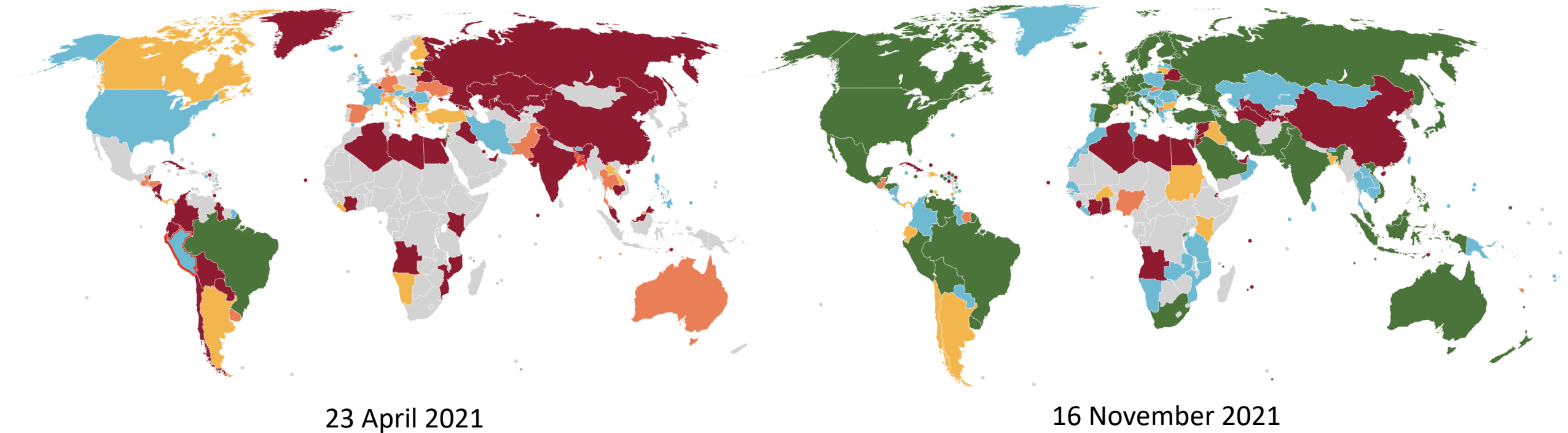
COVID-19 Maternal Immunization Tracker (COMIT) provides:

- a global snapshot of public health policies that influence access to COVID-19 vaccines for pregnant and lactating people.
- maps, tables and country profiles to document the response to the dynamic state of the pandemic and emerging evidence.



*COVID-19 vaccine policies for pregnant and lactating people worldwide.*

# Policies for COVID-19 vaccination during pregnancy have evolved over time



# Acknowledgements



<b>Ruth Faden</b> Principal Investigator Johns Hopkins Berman Institute of Bioethics	<b>Carleigh Krubiner</b> Co-Principal Investigator Johns Hopkins Berman Institute of Bioethics	<b>Ruth Karron</b> Co-Principal Investigator Johns Hopkins Bloomberg School of Public Health
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